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Review Article

Exstrophy Bladder or Ectopia Vesica : 'An Inside Out Affair' A Surgical Update With Review of Current Literature

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Abstract

The word 'exstrophy,' first described by Chaussier in 1780 is derived from the Greek ekstriphein and refers to 'turn inside out'; an uncommon congenital anomaly. It has a male to female ratio of 2:1. These are congenital defects of unknown origin characterised by an abnormal development of multiple systems such as the musculoskeletal system resulting lower abdominal wall muscles separation, the skeletal system resulting in vertebral and spinal cord defects along with a diastasis of the pubic bones leading to the protrusion of hollow organs the bladder & occasionally the intestine that is exposed outside the body. The surgical challenges therefore include the reconstruction of the abdominal wall, the restoration of the bladder to its anatomical position with the aim of having a competent bladder storage system along with a cosmetically acceptable external genital with a good functional sexual outcome. .

Introduction

The first recorded case of bladder exostrophy dates back to Assryo Babyllonian period in the first Millenia. The first description of bladder exostrophy was given by Schenk in 1595. The incidence is quoted as 1 per 100,000 for Americans of Asian origin [1]. It is sporadic, but a genetic component with autosomal dominant inheritance are also described [2]. It affects males approximately twice as often as females [3]. Risk factors include white, non-hispanic maternal ethnicity is a risk factor for bladder exostrophy [4]. A young age and maternal multiparity [5], smoking and irradiation in the first trimester are considered high risk for the development of severe forms of bladder, exstrophy, epispadias complex (BEEC) There is an increase of occurrence of Indirect inguinal hernias due to patent processus vaginalis and large inguinal rings [6]. The consumption of folate decreases the risk of the development of severe forms of BEEC [7].

Exstrophy bladder is a congenital anterior midline defect with the urinary blabber exposed and the genital underdeveloped, it affects both males and female newborns, a part of the BEEC or BEEC spectrum with epispadias of the penis in a male newborn, and in the female an opening located between a divided clitoris should the newborn lie on the mild end of the spectrum this is contrast to severe cloacal exstrophy or OEIS complex (omphalocele, exstrophy, imperforate anus and spinal defects) if the newborn is on the severe end of the spectrum. A non-visualisation of the urinary bladder on prenatal gestational ultrasound as early fifteen weeks and as late as thirty two weeks [8] along with a visual abdominal mass is the first red flag and ought to alert the clinician to this anomaly. Prevention is better than what follows aptly fits this condition as the consequences are profound and follow up lifelong.

Case Report

We report on a 3200 g full-term female neonate who was born with a ventral defect, an exposed bladder everted bladder template that was visible immediately below umbilical stump and normal Apgar Scores. Pregnancy was uneventful, with no fetal anomalies detected at prenatal ultrasound.

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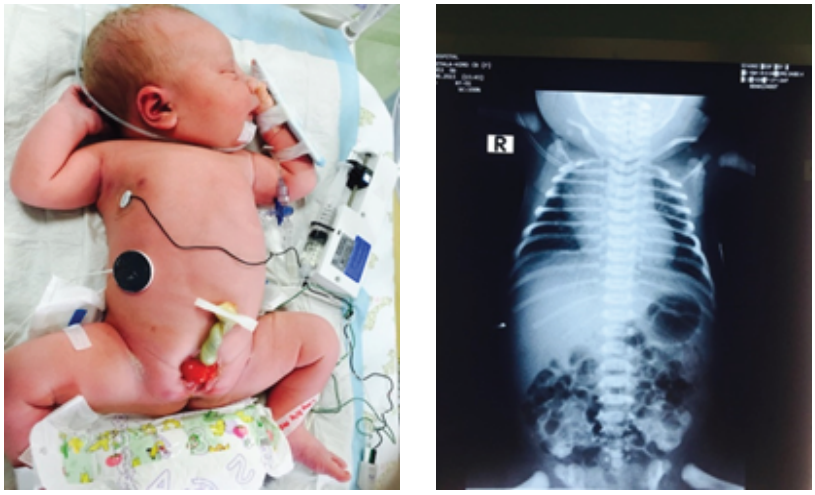

Figure 1. *Triangular defect, exposed bladder, urethral opening, bifid clitoris, anal opening.*

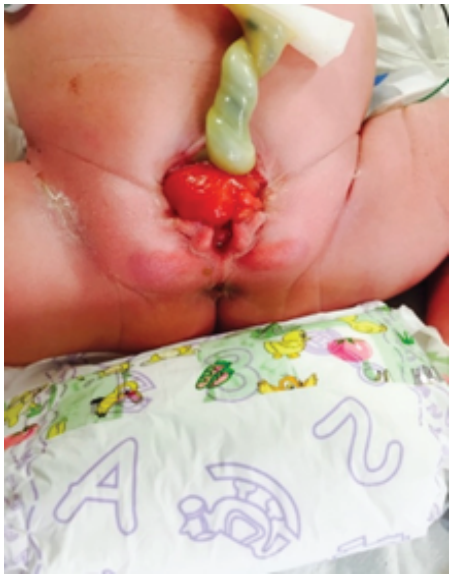

Figure 1. *Anterior infraumbilical triangular defect, exposed bladder with polyps, splayed out genitalia and pubic diastasis. The pubic diastasis palpable at distal end of the triangular edges on either side of the bladder template. In females, a completely split clitoris can be seen next to the open urethral plate. The vaginal opening appears narrow and is placed anteriorly on the perineum. As the anus is ventrally positioned as well, the perineum is shortened.*

The maternal serologies for TORCH infection & hepatitis B surface antigen (HbsAg), hepatitis C virus (HCV), were negative. Delivery was C-section that was not complicated. The neonate presented at birth with a genitourinary defect consistent with the classic bladder exstrophy variant of the exstrophy epispadias complex.

A Prenatal chromosomal analysis revealed a normal 46, XX karyotype.

O.E

Urinary Bladder was small with a diameter of 3 cm with an opened, flattened appearance and a thickened mucosa and stained with urine. The vagina and the anus were anteriorly displaced. The neonate had bifid clitoris with widely spread labia minora and an incomplete umbilicus (Figure 1). Abdominal, renal and spinal ultrasound revealed no other anomaly findings. The bladder was maintained moist by covering it with sterile NaCl 0.9% dressings and a cling wrap (Figure 2). A staged surgical repair was scheduled.

Discussion

Exostrophy of the bladder is a ventral body defect with an incidence of 2/100000 live births [9]. The exact cause of exostrophy of bladder is unknown. The Embryonic theory put forward by Victor F. Marshall and Edward C. Muecke (1968) states that the primary event is failure of mesoderm to migrate between the ectodermal and endodermal layers of the lower abdominal wall at four weeks of intrauterine life and this abnormally large cloacal membrane causes a wedge effect and prevents the medial migration of the mesenchymal tissue. The premature rapture of this cloacal membrane [7,10,11] sets the stage for the development of multiorgan system anomalies. The fluid retention theory by Von Geldern berstungs states

that the cause of exstrophy of the bladder and epispadias is a rupture of the anterior wall of the bladder and the adjacent abdominal wall due to a retention of fluids. The fluid retention is the result of constrictions at various points along the genitourinary tract following obstruction of the urethra or the vesical neck that causes direct pressure of the bladder and separation of the growing pubic bones and the overlying recti abdominis muscles [5]. The rapture of anterior abdominal wall then exposes the growing bladder [12] the pubic diastasis is central to the occurrence of exstrophy bladder, and it precedes exstrophy development [13,14]. The Martinez Frias field defect theory emphasized that exstrophy of the cloaca and exstrophy of the bladder are 2 different expressions of a primary developmental field defect in support of the Opitz's concept that proposes that these biological entities are of idiopathic occurrence characterized by multiple congenital anomalies during blastogenesis. A dysmorphogenetic reaction to a primary field developmental defect [15,16], the cause of exostrophy may thus be early as secondary gastrulation without any involvement of the cloacal membrane. The current molecular and genetic theory has shown that p63 is a member of the p53 tumor suppressor family that is highly expressed in stratified epithelium of the bladder, the insertion and deletion polymorphisms of polymorphic ΔNp63 lead to the reduced p63 expression that produces Exostrophy of bladder [17-21]. If we assume the cloacal membrane wedge theory to be true it is the time and site of rupture of the cloacal membrane that would deem the patient's presentation along the exstrophy epispadias spectrum [10,22,23]. An earlier disruption of the cloacal membrane due to membrane instability especially at four to six week of gestation and prior to fusion of the urorectal septum to the cloacal membrane would result in a severe form of cloacal exstrophy development.

This cloacal exstrophy is characterized by a multisystem anomaly of the genito urinary tract, the musculoskeletal system of lower abdomen and skeletal bony pelvis and spinal meningomyelocele formation [2]. It is thereby a component of the OEIS (omphalocele, exstrophy, imperforate anus, spinal defects) complex [24] and is characterized by a defect of the lower abdominal skin and musculature defect [25] with a diastasis of pubic bone. This diastasis of pubic bones at times has hollow organ protrusion of terminal ileum or even colon some even have a bilobed bladder separated by a portion of cecum between the two hemi bladders [26]. A later disruption of this cloacal membrane following a complete separation of the genitourinary and gastrointestinal (GI) tracts leads to classic bladder exstrophy development. It is the Classical bladder exstrophy that is more common of the two spectrum anomalies. Cloacal exstrophy must be distinguished from the condition of persistent cloaca malformation as this complex anomaly involves incomplete separation of the urinary tract, genital tract, and hindgut and generally no abdominal wall defect is present in persistent cloaca malformation defect. A pseudo exstrophy is a condition that is not common at birth but seen in older age group. The affected children are asymptomatic and continent, their genitalia appear normal. A careful Clinical inspection however reveals a divarication of the rectus abdominis musculature along with pubic symphysis diastasis of various degrees demonstrable on the X-ray pelvis.

On bedside examination the lower abdominal defect externally appears triangular in shape and is bounded by the umbilicus superiorly and inferiorly by a band between the symphysis. The epispadias in a male newborn is along the shaft of a short penis and may be penopubic, penile or glandular in location. The short penis is dorsally curved due to underlying corpus displacement [27]. The glans dorsally that appears like a spade. The urethral plate is open and patulous at the neck of bladder with pubic diastasis and covers the whole dorsum of the penis from the open bladder to the glandular grove. The cryptorchidism occasionally is an associated finding with bladder exstrophy. In the female newborn the labia are divergent with the clitoris split, and the vagina short or stenotic [28]. A minor symphysis gap in bony symphysis is indicative of mild pelvic floor anomaly whereas a wide 5 cm is a finding seen in cloacal exstrophy [29]. The exposed bladder is covered by polyps and is seen dribbling with urine. The shape of the pelvis is wide due to a flattening of levator ani muscle resulting in a box like appearance [30] . The combined pelvic floor design with the levator musculature defect, with the absence of the cardinal ligaments, predisposes women to vaginal or uterine prolapse [31], and even contribute to urinary incontinence. The cause of the fecal incontinence is a malalignment of sphincter complex. The skeletal and limb anomalies include clubfoot deformities, absence of feet, tibial or fibular deformities, and hip dislocations [32]. The spinal defects include vertebral anomalies, scoliosis, myelomeningocele, dysraphism, tethered cord and and spina bifida and are reported at 7% of cases [33]. Abdominal defects include omphaloceles seen in 88% cases umbilical and indirect inguinal hernias. The urological malformations include ureteropelvic junction obstruction, ectopic pelvic kidney, horseshoe kidney, megaureter, ureteral ectopy and ureter. The hind gut anomalies are an anteriorly displaced anus, Imperforate anus, rectal stenosis or prolapse.

Pre-operative workup routine blood investigations, Xray chest and pelvis and spine, ultrasound KUB.

Principles of surgical management

Primary basic care

The application of plastic cling foil or a topical ointment to the bladder plate to prevent the environmental losses of an exposed bladder and the effects of continuous dribbling of urine over the bladder surface.

Multidisciplinary team (MDT)

Involvement of a pediatric urologist or pediatric surgeon. Neonatologist, pediatric gastroenterologist for short gut physiology with parenteral and modified external feeding. An orthopedic surgeon, a neurosurgeon, a child psychiatrist and a counsellor for long term management of urinary continence.

Surgical defect closure can be either performed in a single stage or as a multi staged procedure, depending on the severity of the defect and the facilities at the tertiary care hospital.

Treatment of gastrointestinal (GI) anomalies and myelodysplasia has priority over management of urinary and genital anomalies.

MSRE

Modern staged repair of exstrophy after John Gearhart [8] and is performed within three days of newborn life [32]. MRSE is reported to achieve dryness in more than seventy percent of new borns [29,34]. The aim is to provide outlet resistance to aid urinary bladder growth. Stage one by returning the exposed bladder, the posterior urethra and closure of the abdominal wall. The advantages cited are anatomical for bladder neck and for bladder neck, antireflux reconstruction when bladder

capacity has increased and physiological for bladder cycling with development of bladder musculature. The early return of the bladder additionally provides protection to the exposed bladder mucosa. If the pubic defect small an osteotomy can be avoided. Pelvic osteotomies are transverse bilaterally and vertical posteriorly at the iliac bone. In the case of female newborns also undergo genitoplasty and urethroplasty as a part of the stage one surgery. The reconstruction recommended is using the Woodhouse technique and consists of vaginoplasty including clitoris repair,a vulvoplasty, mons plasty with redistribution of pubic hair [31]. Stage II Repair of epispadias using a modified Cantwell ransley that is performed at six to twelve months of age. The patient's bladder capacity is accessed annually using a gravity cystogram.

Stage III Bladder neck reconstruction and the continent Young Dees-Leadbetter procedure is performed at a time when the child has sufficient bladder capacity of less than 100ml by the age of five to ten year of school age.

Some surgeons perform bladder neck reconstruction before epispadias repair [35]. The reimplantation of ureter is done at this stage to correct the vesicoureteral reflux and the ensuing complications that arise with recurrent UTIs. Those Children who have not achieved urinary continence usually require a augmentation cystoplasty with bladder neck transection procedure. It is the urinary incontinence that is an important indicator of outcome in the long term follow up of bladder exstrophy repair [36,37].

CPRE

The complete repair is named after Michael Mitchell. The traditional and oldest procedure for bladder exstrophy. It aims at the return of the primary bladder with urethroplasty & reconstruction of the genital all in one setting [24]. It addresses the bladder neck and urethra as a single unit and comprises of primary abdominal wall with bladder closure and partial tightening of the bladder neck with epispadias repair [38]. The penile disassembly technique for epispadias repair refers to dissecting the urethral plate from the corporal bodies the division of the intersymphyseal bands, and ensures that vesicourethral unit is buried deep into the pelvis [38]. The reimplantation of bilateral ureteral if performed during this surgery reduces the complications associated with vesicourethral reflux [39]. The advantages include decrease costs and morbidity and posterior positioning of the bladder neck into the pelvis [38]. The decision for a Urinary diversion for classic bladder is done if extremely small bladder plate not suitable for functional closure.

Complete primary repair for classic bladder exstrophy. Mitchell introduced his primary complete bladder closure with simultaneous correction of the epispadias using the penile disassembly technique [38]. Based on the hypothesis that bladder exostrophy results from anterior herniation of the bladder, the operative approach must address the bladder, bladder neck and urethra as a complete unit and move this unit permanently into the pelvis. Mitchell impressively demonstrated that penile dissection into its three components (two corpora cavernosa and the corpus spongiosum) ensures blood flow in each component and that the penis can be reassembled in an anatomically fashion [38]. The proponents of early bladder closure done within day three of life, argue it favours sooner bladder cycling and improved bladder musculature function. The closure of the pelvic diastasis is feasible as the bones are malleable thereby avoiding the need for osteotomy. If the bladder plate is adequate, reclosure with pelvic osteotomies is recommended. In this instance, bladder closure and epispadias repair are performed in one stage. Urinary diversion is the alternative therapy, should the bladder plate be small.

A prolonged exposure of bladder to environmental agents is a predisposer to premalignancy [17], an equal number of studies have refuted this claim [39].

The complete primary repair combines primary abdominal wall and bladder closure with epispadias repair and partial tightening of the bladder neck [38] addressing the bladder, bladder neck and urethra as a single unit. Those favoring CRPE site cost and a decrease the morbidity associated with multiple surgical procedures and the procedure is reported to stimulate bladder growth. The epispadias is addressed by dissecting the urethral plate from the corporal bodies as "penile disassembly" technique [40]. It is interesting to note that the long-term urinary continence with CPRE is comparable to MSRE [37].

Complications

These include Immediate and delayed, Minor and Major complications. Clinical problems related to poor emptying include recurrent febrile urinary tract infection, persistent vesicoureteral reflux due to excessive outlet resistance and high pressure in a small-capacity reservoir. Abnormal bladder function may result in poor emptying. Epididymitis, bladder stones, acute urinary retention, and ischemia of bladder mucosa, rupture of the native bladder even bladder prolapse, fistulas vesicocutaneous, urethrocutaneous. If spontaneous closure does not occur, surgical repair is warranted.

Loss of the hemiglans or corporal body has been reported as a result of complete primary repair [32]. Osteotomy related complications, Short gut syndrome and Persistent incontinence a lifelong serial follow up in clinic.

The role of prenatal counselling

Is imperative considering the quality of life, long term prognosis in adults affected by bladder exstrophy, particularly in regard to urinary continence, and sexual and reproductive issues in growing male and female counterparts.

Conclusion

The affair is definitely a complicated one and retrospectively it is the non visualization of the bladder on the prenatal ultrasound that is the earliest red flag that should alert the examining clinician. The role of prenatal scans cannot be overemphasised. Family counselling about the complexity this anomaly is important especially if gender assignment procedures are under taken and a lifelong care is involved.

Declaration of consent

Appropriate patient consent forms were obtained.

Conflict of interest

None

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References

1. James LM, Erickson JD, Mc Clearn AB. Prevalence of birth defects. Division of Birth Defects and Developmental

Disabilities; National Center for Enviromental Health; Centers for Disease Control and Prevention, Atlanta, Georgia; 1999.

2. Froster UG, Heinritz W, Bennek J, Horn LC, Faber R. Another case of autosomal dominant exstrophy of the bladder. Prenat Diagn. 2004;24(5):375-377.
3. Gambhir L, Höller T, Müller M, et al. Epidemiological survey of 214 families with bladder exstrophy-epispadias complex. J Urol. 2008;179(4):1539-1543.
4. Caton AR, Bloom A, Druschel CM, Kirby RS. Epidemiology of bladder and cloacal exstrophies in New York State, 1983-1999. Birth Defects Res A Clin Mol Teratol. 2007;79:781–787.
5. Nelson CP, Dunn RL, Wei JT. Contemporary epidemiology of bladder exstrophy in the United States. J Urol. 2005;173(5):1728-1731.
6. Diamond DA, Jeffs RD. Cloacal exstrophy: a 22-year experience. J Urol. 1985;133(5):779-782.
7. Ebert AK, Schott G, Bals-Pratsch M, Seifert B, Rösch W H. Long-term follow-up of male patients after reconstruction of the bladder-exstrophy-epispadias complex: psychosocial status, continence, renal and genital function. J Pediatr Urol. 2010;6(1):6–10.
8. Ebert AK, Reutter H, Ludwig M, Rösch WH. The exstrophy-epispadias complex. Orphanet J Rare Dis. 2009;4:23.
9. Grady RW, Mitchell ME. Complete primary repair of exstrophy. J Urol. 1999;162(4):1415-1420.
10. Marshall VF, Muecke EC. Variation in exstrophy of the bladder. J Urol. 1962;88:766.
11. Patten BM, Barry A. The genesis of exstrophy of the bladder and epispadias. Am J Anat. 1952;90(1):35-57.
12. Von Geldern, Charles E. Etiology of exstrophy of bladder. Arch Surg. 1924;8:61.
13. Reutter H, Boyadjiev SA, Gambhir L, et al. Phenotype severity in the bladder exstrophy-epispadias complex: analysis of genetic and nongenetic contributing factors in 441 families from North America and Europe. J Pediatr. 2011;159(5):825-831.e1.
14. Braga LH, Lorenzo AJ, Jrearz R, Bagli DJ, Salle JL. Bilateral ureteral reimplantation at primary bladder exstrophy closure. J Urol. 2010;183(6):2337-2341.
15. Cadeddu JA, Benson JE, Silver RI, Lakshmanan Y, Jeffs RD, Gearhart JP. Spinal abnormalities in classic bladder exstrophy. Br J Urol. 1997;79(6):975-978.
16. Martínez-Frías ML. Primary midline developmental field. I. Clinical and epidemiological characteristics. Am J Med Genet. 1995;56(4):374-381.
17. Ambrose SS, O'Brien DP 3rd. Surgical embryology of the exstrophy-epispadias complex. Surg Clin North Am. 1974;54(6):1379-1390
18. Dodson JL, Surer I, Baker LA, Jeffs RD, Gearhart JP. The newborn exstrophy bladder inadequate for primary closure: evaluation, management and outcome. J Urol. 2001;165(5):1656-1659.
19. Stockard CR. Developmental rate and structural expression and experimental study of twins double monsters and single deformities and the interaction among embryonic organs during their origin and development. Am J Anat. 1921;28:112–277.
20. Porter RM. Bladder outside the belly. Nashville J Med And Surg. 1855;8:381.
21. Kulkarni B, Chaudhari N. Embryogenesis of bladder exstrophy: A new hypothesis. J Indian Assoc Pediatr Surg. 2008;13(2):57-60.
22. Baird AD, Nelson CP, Gearhart JP. Modern staged repair of bladder exstrophy: a contemporary series. J Pediatr Urol. 2007;3(4):311–5.
23. Muecke EC. The role of the cloacal membrane in exstrophy: The first successful experimental study. J Urol. 1964;92:659-667.
24. Grady RW, Mitchell ME. Management of epispadias. Urol Clin North Am. 2002;29(2):349-vi.
25. Schrott KM. Komplette einaktige Aufbauplastik der Blasen-exstrophie. Plastisch-rekonstruktive Chirurgie in der Urologie 1999;430-438.
26. Siffel C, Correa A, Amar E, et al. Bladder exstrophy: an epidemiologic study from the International Clearinghouse for Birth Defects Surveillance and Research, and an overview of the literature. Am J Med Genet C Semin Med Genet. 2011;157C(4):321-332.
27. Stec AA, Tekes A, Ertan G, et al. Evaluation of pelvic floor muscular redistribution after primary closure of classic bladder exstrophy by 3-dimensional magnetic resonance imaging. J Urol. 2012;188(4 Suppl):1535-1542.
28. Silver RI, Yang A, Ben-Chaim J, Jeffs RD, Gearhart JP. Penile length in adulthood after exstrophy reconstruction. J Urol. 1997;157(3):999-1003.
29. Ko JS, Lue K, Friedlander D, et al. Cystectomy in the Pediatric Exstrophy Population: Indications and Outcomes. Urology. 2018;116:168-171.
30. Connolly JA, Peppas DS, Jeffs RD, Gearhart JP. Prevalence and repair of inguinal hernias in children with bladder exstrophy. J Urol. 1995;154(5):1900-1901.
31. Woodhouse CRJ, Hinsch R. The anatomy and reconstruction of the adult female genitalia in classical exstrophy. BJU. 1997;79:618–622.
32. Gearhart JP. The bladder exstrophy-epispadias-cloacal exstrophy complex. In: Gearhart JP, Rink RC, Mouriquand PDE, editor. Pediatric Urology. Chapter 32. Philadelphia: W. B. Saunders Co; 2001. pp. 511–546.
33. Ansari MS, Gearhart JP, Cervellione RM, Sponseller PD. The application of pelvic osteotomy in adult female patients with exstrophy: applications and outcomes. BJU Int. 2011;108(6):908-912.
34. Opitz JM. Blastogenesis and the "primary field" in human development. Birth Defects Orig Artic Ser. 1993;29(1):3-37.
35. K V SK, Mammen A, Varma KK. Pathogenesis of bladder exstrophy: A new hypothesis. J Pediatr Urol. 2015;11(6):314-318.
36. Chan DY, Jeffs RD, Gearhart JP. Determinants of continence in the bladder exstrophy population: predictors of success?. Urology. 2001;57(4):774-777.
37. Baird A D, Sponseller P D, Gearhart J P. The place of pelvic osteotomy in the modern era of bladder exstrophy reconstruction. J Pediatr Urol. 2005;1(1):31–36.
38. Bhatnagar V. The management of bladder exstrophy: Indian scenario. J Indian Assoc Pediatr Surg. 2011;16(2):43-44.
39. Wilkins S, Zhang KW, Mahfuz I, et al. Insertion/deletion polymorphisms in the ΔNp63 promoter are a risk factor for bladder exstrophy epispadias complex. PLoS Genet. 2012;8(12):e1003070.
40. Baka-Jakubiak M. Combined bladder neck, urethral and penile reconstruction in boys with exstrophy-epispadias complex. BJU. 2000;86:513–518.